

## HEAVY METALS AND COUPLE FECUNDITY, THE LIFE STUDY

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**Background and Aims:** Exposure to high concentrations of heavy metals has been associated with a spectrum of adverse reproductive outcomes in men and women. However, limited prospective study has focused on the relation between environmentally relevant concentrations and human fecundity serving as the impetus for the study.

**Methods:** Using population based sampling frameworks, we recruited 501 couples discontinuing contraception for the purpose of becoming pregnant in two geographic regions with reported exposure to persistent environmental pollutants including metals. Upon enrollment into the cohort, couples completed baseline interviews and anthropometric assessments and provided blood specimens for the quantification three metals (i.e., cadmium (ng/ml), mercury (ng/ml), lead (ug/dl)) using inductively coupled plasma mass spectrometry. Couples completed daily journals on intercourse and lifestyle behaviors along with menstruation and pregnancy test results for women. Couples were followed until an hCG pregnancy or 12 cycles without pregnancy. Fecundability odds ratios (FORs) and 95% confidence intervals (CIs) were estimated adjusting for maternal age, body mass index, cotinine, and serum lipids in relation to female then male exposures. FORs <1 reflect reduced fecundity or a longer time-to-pregnancy. Final models included both partners' metals concentrations along with relevant covariates.

**Results:** In adjusted models, cadmium was associated with reduced FORs for both female (0.82; 95% CI 0.69-0.99) and male (0.84; 95% CI 0.71-0.99) exposure. Lead was associated with a significant reduction in the FOR (0.86; 95% CI 0.75-0.98), but only for male exposure. In the joint analysis, male lead concentration significantly reduced the FOR (0.86; 95% CI 0.76-0.99). No association was observed for mercury and couple fecundity.

**Conclusions:** This prospective couple based cohort with longitudinal capture of time-to-pregnancy affirms the reproductive toxicity of cadmium and lead concentrations for environmentally relevant concentrations underscoring the importance of measuring both partner's exposures for coupled based reproductive outcomes.